

Please amend page 20, line 1 as follows:

Claims What is claimed is:

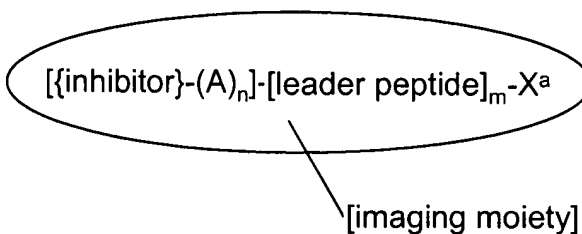
This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) An imaging agent which comprises a synthetic caspase-3 inhibitor labelled with an imaging moiety, wherein the caspase-3 inhibitor has a K_i for caspase-3 of less than 2000 nM, and wherein following administration of said labelled caspase-3 inhibitor to the mammalian body *in vivo*, the imaging moiety can be detected either externally in a non-invasive manner or *via* use of detectors designed for use *in vivo*
2. (Cancel) The imaging agent of Claim 1, where the synthetic caspase-3 inhibitor has a K_i for caspase-3 of less than 500 nM.
3. (Currently amended) The imaging agent of ~~Claims 1 or 2~~Claim 1, where the synthetic caspase-3 inhibitor has a molecular weight of 150 to 3000 Daltons.
4. (Currently amended) The imaging agent of ~~Claims 1 to 3~~Claim 1, where the imaging moiety comprises:
 - (i) a radioactive metal ion;
 - (ii) a paramagnetic metal ion;
 - (iii) a gamma-emitting radioactive halogen;
 - (iv) a positron-emitting radioactive non-metal;
 - (v) a hyperpolarised NMR-active nucleus;
 - (vi) an optical dye suitable for *in vivo* imaging.
5. (Currently amended) The imaging agent of ~~claims 1 to 4~~Claim 1, which further comprises a 4 to 20-mer leader peptide sequence, wherein said leader peptide

facilitates cell membrane transport from the outside to the inside of a mammalian cell *in vivo*.

6. (Currently amended) The imaging agent of Claim 5 where the synthetic caspase-3 inhibitor conjugate is of Formula I:



(Formula I)

where:

{inhibitor} is ~~the~~ a caspase-3 inhibitor with a K_i for caspase-3 of less than 2000 nM of claims 1 to 3;

[leader peptide] is as defined in Claim [4] 5 and is attached by either its' amine or carboxyl terminus;

-(A)_n- is a linker group wherein each A is independently -CR₂-, -CR=CR-, -C≡C-, -CR₂CO₂-, -CO₂CR₂-, -NRCO-, -CONR-, -NR(C=O)NR-, -NR(C=S)NR-, -SO₂NR-, -NRSO₂-, -CR₂OCR₂-, -CR₂SCR₂-, -CR₂NRCR₂-, a C₄₋₈ cycloheteroalkylene group, a C₄₋₈ cycloalkylene group, a C₅₋₁₂ arylene group, or a C₃₋₁₂ heteroarylene group, an amino acid or a monodisperse polyethyleneglycol (PEG) building block;

R is independently chosen from H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxyalkyl or C₁₋₄ hydroxyalkyl;

n is an integer of value 0 to 10,

m is 0 or 1;

and X^a is H, OH, Hal, NH₂, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkoxyalkyl, C₁₋₄ hydroxyalkyl or X^a is the imaging moiety.

7. (Currently amended) The imaging agent of ~~Claims 1 to 6~~Claim 1, where the radioactive metal ion is a gamma emitter or a positron emitter.

8. (Original) The imaging agent of Claim 7, where the radioactive metal ion is ^{99m}Tc , ^{111}In , ^{64}Cu , ^{67}Cu , ^{67}Ga or ^{68}Ga .
9. (Currently amended) The imaging agent of ~~Claims 1 to 6~~Claim 1, where the paramagnetic metal ion is Gd(III), Mn(II) or Fe(III).
10. (Currently amended) The imaging agent of ~~Claims 1 to 6~~Claim 1, where the gamma-emitting radioactive halogen is ^{123}I .
11. (Currently amended) The imaging agent of ~~Claims 1 to 6~~Claim 1, where the positron-emitting radioactive non-metal is chosen from ^{18}F , ^{11}C , ^{124}I or ^{13}N .
12. (Currently amended) The imaging agent of ~~Claims 1 to 11~~Claim 1, where the synthetic caspase-3 inhibitor comprises one or more of the caspase-3 inhibitors defined in (i) to (ix):
 - (i) a tetrapeptide derivative of Formula III

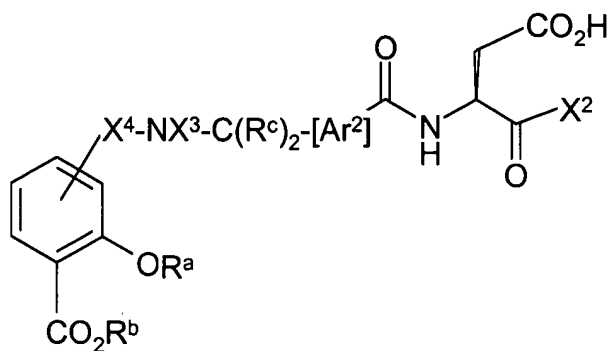
$$\text{Z}^1\text{-Asp-Xaa1-Xaa2-Asp-X}^1 \quad (\text{III})$$
 where Z^1 is a metabolism inhibiting group attached to the N-terminus of the tetrapeptide;

Xaa1 and Xaa2 are independently any amino acid;

X^1 is an $-\text{R}^1$ or $-\text{CH}_2\text{OR}^2$ group attached to the carboxy terminus of the tetrapeptide;

where R^1 is H, $-\text{CH}_2\text{F}$, $-\text{CH}_2\text{Cl}$, C_{1-5} alkyl, C_{1-5} alkoxy or $-(\text{CH}_2)_q\text{Ar}^1$, where q is an integer of value 1 to 6 and Ar^1 is C_{6-12} aryl, C_{5-12} alkyl-aryl, C_{5-12} fluoro-substituted aryl, or C_{3-12} heteroaryl;

R^2 is C_{1-5} alkyl, C_{1-10} acyl or Ar^1 ;
 - (ii) a quinazoline or anilinoquinazoline;
 - (iii) a 2-oxindole sulphonamide;
 - (iv) an oxoazepinoindoline;
 - (v) a compound of Formula IV



(IV)

where X^2 is H, C_{1-5} alkyl or $-(CH_2)_r-(S)_s-(CH_2)_tAr^3$, where r and t are integers of value 0 to 6, s is 0 or 1 and Ar^3 is C_{6-12} aryl, C_{5-12} alkyl-substituted aryl, C_{5-12} halo-substituted aryl, or C_{3-12} heteroaryl;

Ar^2 is C_{6-12} aryl or C_{3-12} heteroaryl;

X^3 is an R^b group;

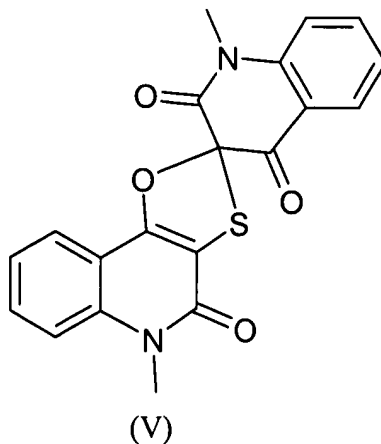
X^4 is $-SO_2-$ or $-CR_2-$

R^a is H, C_{1-5} alkyl or P^{GP} where P^{GP} is a protecting group;

R^b is an R^a group or C_{1-5} acyl;

each R^c is independently H or C_{1-5} alkyl;

(vi) a compound of Formula V



(V)

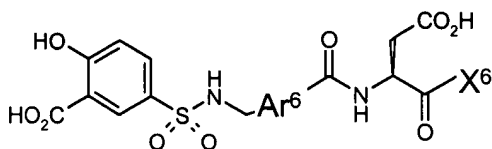
(vii) a pyrazinone;

(viii) a dipeptide of Formula VI:



where the $\text{-CH}_2\text{SR}^1$ group is attached to the carboxy terminus of the dipeptides, and Z^1 and R^1 are as defined for Formula (III);

(ix) a salicylic acid sulphonamide of Formula XI:



Formula XI

Where Ar⁶ is a 5 or 6-membered C₄₋₆ aryl or heteroaryl ring, and X⁶ is H or $\text{-CH}_2\text{SR}^2$, where R² is as defined above.

13. (Original) The imaging agent of Claim 12, where the synthetic caspase-3 inhibitor comprises:

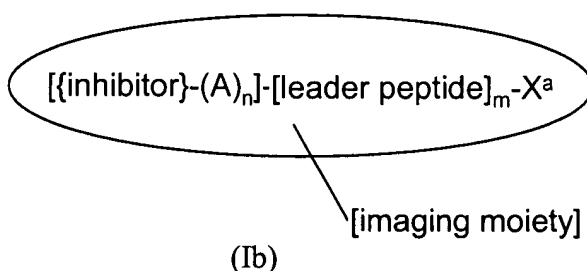
- (i) a tetrapeptide of Formula III; or
- (ii) a 2-oxindole sulphonamide; or
- (iii) a dipeptide of Formula VI.

14. (Currently amended) The imaging agent of ~~Claims 1 to 13~~ Claim 1, where the synthetic caspase-3 inhibitor is selective for caspase-3 over caspase-1, by a factor of at least 50.

15. (Currently amended) The imaging agent of ~~Claims 13 or 14~~ Claim 13, where the synthetic caspase-3 inhibitor comprises a tetrapeptide of Formula III or a dipeptide of Formula VI.

16. (Currently amended) A pharmaceutical composition which comprises the imaging agent of ~~claims 1 to 15~~ Claim 1 together with a biocompatible carrier, in a form suitable for mammalian administration.

17. (Currently amended) A radiopharmaceutical composition which comprises the imaging agent of ~~claims 1 to 15~~ Claim 1 wherein the imaging moiety is radioactive, together with a biocompatible carrier, in a form suitable for mammalian administration.
18. (Original) The radiopharmaceutical composition of claim 17, where the imaging moiety comprises a positron-emitting radioactive non-metal or a gamma-emitting radioactive halogen.
19. (Original) The radiopharmaceutical composition of claim 17, where the imaging moiety comprises a radioactive metal ion.
20. (Currently amended) A conjugate of a synthetic caspase-3 inhibitor with a ligand, wherein the caspase-3 inhibitor has a K_i for caspase-3 of less than ~~2000~~ 500 nM, and wherein said ligand is capable of forming a metal complex with a radioactive or paramagnetic metal ion.
21. (Currently amended) The conjugate of Claim 20, of Formula Ib:



where ~~A, n, m and X^a are as defined in Claim 6~~

-(A)_n- is a linker group wherein each A is independently -CR₂-, -CR=CR-, -C≡C-, -CR₂CO₂-, -CO₂CR₂-, -NRCO-, -CONR-, -NR(C=O)NR-, -NR(C=S)NR-, -SO₂NR-, -NRSO₂-, -CR₂OCR₂-, -CR₂SCR₂-, -CR₂NRCR₂-, a C₄₋₈ cycloheteroalkylene group, a C₄₋₈ cycloalkylene group, a C₅₋₁₂ arylene group,

or a C₃₋₁₂ heteroarylene group, an amino acid or a monodisperse polyethyleneglycol (PEG) building block;

R is independently chosen from H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxyalkyl or C₁₋₄ hydroxyalkyl;

n is an integer of value 0 to 10,

m is 0 or 1;

and X^a is H, OH, Hal, NH₂, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkoxyalkyl, C₁₋₄ hydroxyalkyl or X^a is the imaging moiety.

22. (Currently amended) The conjugate of ~~Claims 20 or 21~~Claim 20, wherein the ligand is a chelating agent.
23. (Original) The conjugate of Claim 22, wherein the chelating agent has a diaminedioxime, N₂S₂, or N₃S donor set.
24. (Currently amended) A kit for the preparation of the radiopharmaceutical composition of Claim 19, which comprises the conjugate of a synthetic caspase-3 inhibitor with a ligand, wherein the caspase-3 inhibitor has a K_i for caspase-3 of less than 500 nM, and wherein said ligand is capable of forming a metal complex with a radioactive or paramagnetic metal ion.~~Claims 20 to 23.~~
25. (Original) The kit of Claim 24, where the radioactive metal ion is ^{99m}Tc, and the kit further comprises a biocompatible reductant.
26. (Currently amended) A kit for the preparation of the radiopharmaceutical composition of Claim 18, which comprises a precursor, said precursor being a non-radioactive derivative of ~~the~~ a caspase-3 inhibitor of claims 1 to 15, wherein the caspase-3 inhibitor has a K_i for caspase-3 of less than 2000 nM, wherein said non-radioactive derivative is capable of reaction with a source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen to give the desired radiopharmaceutical.

27. (Original) The kit of claim 26 where the precursor is in sterile, apyrogenic form.
28. (Currently amended) The kit of ~~Claims 26 or 27~~Claim 26, where the source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen is chosen from:
- (i) a halide ion or F^+ or I^+ ; or
 - (ii) b an alkylating agent chosen from an alkyl or fluoroalkyl halide, tosylate, triflate or mesylate;
29. (Currently amended) The kit of ~~Claims 26 to 28~~Claim 26, where the non-radioactive derivative is chosen from:
- (i) a an organometallic derivative such as a trialkylstannane or a trialkylsilane;
 - (ii) b a derivative containing an alkyl halide, alkyl tosylate or alkyl mesylate for nucleophilic substitution;
 - (iii) c a derivative containing an aromatic ring activated towards nucleophilic or electrophilic substitution;
 - (iv) d a derivative containing a functional group which undergoes facile alkylation;
 - (v) e a derivative which alkylates thiol-containing compounds to give a thioether-containing product.
30. (Currently amended) The kit of ~~claims 26 to 29~~claim 26, where the precursor is bound to a solid phase.
31. (Currently amended) Use of the imaging agent of ~~claims 1 to 15~~Claim 1 in a method of diagnosis of a caspase-3 implicated disease state of the mammalian body, wherein said mammal is previously administered with the pharmaceutical composition which comprises the imaging agent of Claim 1 together with a biocompatible carrier, in a form suitable for mammalian administration ~~of claim 16,~~

or the radiopharmaceutical composition which comprises the imaging agent of Claim 1 wherein the imaging moiety is radioactive, together with a biocompatible carrier, in a form suitable for mammalian administration ~~of claims 17 to 19.~~